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EXAMINER	
YOUNG, SHAWQUIA	

ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,067	BOIVIN ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-22,37-46,66,81-88,108 and 119-129* is/are pending in the application.

4a) Of the above claim(s) *84-88,108 and 119-126* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-22,37-46,66,81-83 and 127-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-22, 37-46, 66, 81-88, 108 and 119-129 are currently pending in the instant application. Applicants have cancelled claim 2 and added new claims 127-129 in an amendment filed on June 16, 2008.

I. *Response to Arguments/Remarks*

Applicants' amendment, filed June 16, 2008, has overcome the rejection of claims 1, 3-8, 22 and 81-83 under 35 USC 112, second paragraph as being indefinite for the phrase "has the structure"; the rejection of claims 1-22, 37, 66 and 81-83 under 35 USC 112, first paragraph as failing to comply with the written description requirement and the objection to the oath. The above rejections and objection have been withdrawn.

The Examiner has maintained the rejection of claims 9-21, 37-46 and 66 under 35 USC 112, second paragraph as being indefinite for the phrase "has the structure" because Applicants have failed to amend the phrase in claims 9 and 15.

The Examiner has maintained the objection of claims 1, 3-22, 37-46, 66 and 81-83 as containing non-elected subject matter. Applicants have failed to delete all of the non-elected subject matter such as "R_8 and R_9 can, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms".

The Examiner has maintained the ODP rejection of claims 1, 3-22, 40, 43, 66 and 81 as being unpatentable over claims 1-5 and 10 of copending US application 10/657,910 because Applicants have failed to file a terminal disclaimer.

II. *Rejection(s)*

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

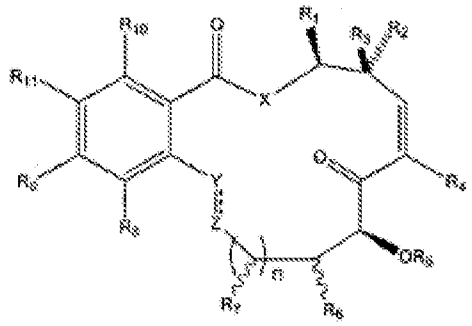
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-22, 40, 43, 66 and 81 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 10 of copending US application 10/657,910. This is a provisional obviousness-type double patenting rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

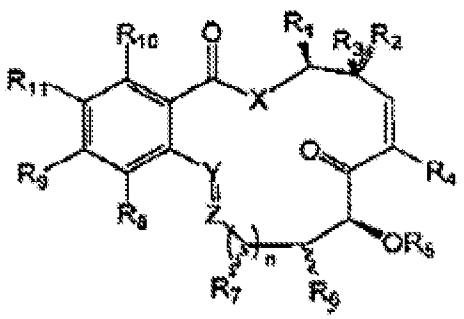
Applicants' elected subject matter is a compound of formula I



, wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic or aryl; R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, aliphatic, heteroaliphatic, alicyclic, or aryl; or R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms or R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; R_4 is hydrogen or halogen; R_5 is hydrogen, an oxygen protecting group or prodrug moiety; R_6 is hydrogen, hydroxyl or protected hydroxyl; n is 0-2; R_7 or each occurrence, is independently hydrogen, hydroxyl or protected hydroxyl; R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12} or $NR_{12}R_{13}$; R_9 is $NR_{12}R_{13}$; wherein R_{12} and R_{13} are independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, aryl or a protecting group; R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino or protected amino; R_{11} is hydrogen, hydroxyl or protected hydroxyl; X is absent or is O, NH, N-alkyl, CH_2 or S and Y and Z are defined as in claim 1.

Determining the Scope and Content of the Copending Application

Claim 1 of the copending application claims a pharmaceutical composition comprising a compound of the formula



, wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic or aryl; R_2 is methyl; R_3 is hydrogen, halogen, hydroxyl, protected hydroxyl, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; R_4 is hydrogen or halogen; R_5 is hydrogen or an oxygen protecting group; R_6 is hydrogen, hydroxyl or protected hydroxyl; n is 0-2; R_7 or each occurrence, is independently hydrogen, hydroxyl or protected hydroxyl; R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12} or $NR_{12}R_{13}$; R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}; SR_{12}, $NR_{12}R_{13}$, $X_1(CH_2)_pX_2$-R_{14} or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino or $–X_1(CH_2)_pX_2$-R_{14}; wherein R_{12} and R_{13} are independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl,heteroaryl or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3

nitrogen or oxygen atoms and each of R_{12} and R_{13} are optionally further substituted as defined in claim 1; R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino or protected amino; R_{11} is hydrogen, hydroxyl or protected hydroxyl; X is absent or is O, NH or CH_2 and Y and Z are defined as in claim 1.

Ascertaining the Differences Between the Instant Application and the Copending Application

The claims of the instant application are drawn to a broader compound genus than the claims of the copending application, which encompass the elected subject matter of the copending application. In the instant application, X is absent or is O, NH, N-alkyl, CH_2 or S whereas in the copending application X is O.

Finding Prima Facie Obviousness

As mentioned above, the genus compound of the instant application encompasses the narrower genus compound in the copending application. Therefore, one of ordinary skill in the art would be motivated to prepare and claim the scope of the compounds in the instant application since the scope already in the copending application is encompassed by the scope of the elected subject matter in the instant claims. As a result, the claims are rejected under obviousness-type double patenting.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-21, 37-46 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "having the structure" or "has the structure" renders the products indefinite as the term the phrase "having the structure" or "has the structure" can be considered open-ended language when not clearly defined and therefore is including additional subject matter in the compounds of the formula I that is not described in the instant specification and is not particularly pointed out or distinctly claimed. A claim to a chemical compound cannot be open-ended, but must be claimed with precision. This rejection can be overcome by amending the phrase "having the structure" or "has the structure" to read "of the structure" in claims 9 and 15.

Claims 1, 3-22, 37-46, 66, 81-83 and 127-129 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "may form….." in the definition of variables R_1 and R_3, R_1 and R_2, and R_8 and R_9 renders the products indefinite as the phrase "may form..." can be considered open-ended language when not clearly defined and therefore is including additional subject matter in the compounds of the formula I that is not described in the instant specification

and is not particularly pointed out or distinctly claimed. A claim to a chemical compound cannot be open-ended, but must be claimed with precision. This rejection can be overcome by amending the phrase "may form…." to read "form…." in claims 1, 3-22, 37-46, 66, 81-83 and 127-129.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is a pharmaceutical composition wherein the compound is present in an amount effective to inhibit AP-1 activation and a pharmaceutical composition wherein the compound is present in an amount effective to inhibit a protein kinase.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the

art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since Applicants are claiming that the claimed compounds can inhibit AP-1 activation and all protein kinases.

For example, Applicants' claims are drawn to a composition which comprises a compound in an amount effective to inhibit a protein kinase. It is the state of the prior art that a protein kinase is a kinase enzyme that modifies other proteins by chemically adding phosphate groups to them. The class of protein kinase may further be separated into subsets of PKC alpha, PKC beta and PKC gamma, each with specific functions. There are various classes of protein kinases such as serine/threonine-specific protein kinases (i.e. MAP kinase), tyrosine-specific protein kinases (i.e. JAK), histidine-specific protein kinases, etc. The term "protein kinase" is considered broad and embraces vast subject matter that is not supported by Applicants' specification. (See URL; http://en.wikipedia.org/wiki/Protein_kinase)

The amount of direction present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. There are no working examples present for the inhibition of AP-1 activation and a protein kinase.

Test assays and procedure are provided in the specification at pages 376-377 for the inhibition of NF-κB activation. Receptor activity is generally unpredictable and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to which of the claimed compounds can inhibit AP-1 activation and protein kinases.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to a pharmaceutical composition wherein the compound is present in an amount of effective to inhibit AP-1 activation and any protein kinase.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which claimed compounds would inhibit AP-1 activation and any protein kinase.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity. The specification fails to provide sufficient support of the broad use of the claimed compounds of the invention as inhibitors of AP-1 activation and any protein kinase. As a result necessitating one of skill to perform an exhaustive search for which protein kinases and AP-1 activation can be inhibited by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to

engage in undue experimentation to test which protein kinases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the composition claims.

Claims 42 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is drawn to a pharmaceutical composition wherein the compound is present in an amount effective to inhibit proliferation of cancerous cells and angiogenesis on solid tumors or a pharmaceutical composition wherein the compound is present in an amount effective to prevent restenosis.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is

the more specific enablement is necessary in order to satisfy the statute.

For example, Applicants' claims are drawn to a pharmaceutical composition wherein the compound is present in an amount effective to inhibit proliferation of cancerous cells and angiogenesis on solid tumors.

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. Cancer is a disease characterized by a population of cells that grow and divide without respect to normal limits, invade and destroy adjacent tissues, and may spread to distant anatomic sites through a process called metastasis (URL:http://en.wikipedia.org/wiki/ Cancer>). Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast. Symptoms and treatment depend on the cancer type and how advanced it is (URL: <http://www.nlm.nih.gov/medlineplus/cancer.html>>). It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Treatment may include surgery, radiation, chemotherapy, immunotherapy, monoclonal antibody therapy, etc. Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91)

that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols. Because "cancer" refers to a class of diseases, it is unlikely that there will ever be a single "cure or treatment for cancer".

The amount of direction present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. There are no working examples present for the inhibition of the proliferation of cancerous cells and angiogenesis on solid tumors or prevention of restenosis.

Test assays and procedure are provided in the specification at pages 376-377 for the inhibition of NF-κB activation are generally unpredictable and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.” See In re

Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to a pharmaceutical composition wherein the compound is present in an amount effective to inhibit proliferation of cancerous cells and angiogenesis on solid tumors or a pharmaceutical composition wherein the compound is present in an amount effective to prevent restenosis.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all conditions would be benefited by the activity of the claimed compounds and would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of the diseases.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The specification fails to provide sufficient support of the broad use of the claimed compounds of the invention to be used as a medicament. As a result necessitating one of skill to perform an exhaustive search for which diseases can be

treated by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting claims 42 and 46.

Claims 81-83 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining

whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is drawn to a topical pharmaceutical composition for treating or preventing UVB-induced photodamage.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in

the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is necessary in order to satisfy the statute.

The state of the prior art is that sun exposure causes most of the skin changes that we think of as normal part of aging. Over time, the sun's UV light damages the fibers in the skin called elastin. When these fibers breakdown, the skin also bruises and tears more easily-taking longer to heal. Exposure to the sun causes: pre-cancerous and cancerous skin lesions, benign tumors, fine and coarse wrinkles, freckles, etc. UV radiation from the sun is the number one cause of skin cancer but UV light from tanning beds is just as harmful. Cumulative sun exposure causes mainly basal cell and squamous cell skin cancer while episodes of severe sunburns can cause melanoma later in life. Treatment of skin cancer is individualized and is determined by the type of skin cancer, its size and location, etc. Nothing can completely undo sun damage, although the skin can sometimes repair itself.

(See URL, http://www.medicinenet.com/script/main/art.asp?li=USA&articlekey=43077)

The amount of direction present and the presence or absence of working

examples

The only direction or guidance present in the instant specification is minimal. There are no working examples present for the prevention or treatment of the various conditions that are embraced by the term "UVB-induced photodamage".

Test assays and procedure are provided in the specification at pages 376-377 for the inhibition of NF-κB activation are generally unpredictable and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.” See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to a topical pharmaceutical composition for preventing or treating UVB-induced photodamage.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what conditions caused by photodamage would be benefited by the activity of the claimed compounds and would furthermore then have to

determine which of the claimed compounds in the instant invention would provide treatment for the different conditions caused by photodamage.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The specification fails to provide sufficient support of the broad use of the claimed compounds of the invention to be used in the treatment or prevention of UVB-induced photodamage. As a result necessitating one of skill to perform an exhaustive search for which diseases or conditions can be treated by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting claims 81-83.

III. *Objections*

Claim Objection-Non Elected Subject Matter

Claims 1, 3-22, 37-46, 66, 81-83 and 127-129 are objected to as containing non-elected subject matter. To overcome this objection, Applicant should submit an amendment deleting the non-elected subject matter.

IV. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Shawquia Young/

Examiner, Art Unit 1626

/Kamal A Saeed, Ph.D./

Primary Examiner, Art Unit 1626